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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,934	02/24/2006	John W Harmon	001107.00550	3384
22907 7590 09/27/2007 BANNER & WITCOFF, LTD. 1100 13th STREET, N.W. SUITE 1200 WASHINGTON, DC 20005-4051			EXAMINER ZARA, JANE J	
			ART UNIT 1635	PAPER NUMBER
			MAIL DATE 09/27/2007	DELIVERY MODE PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

**Office Action Summary**

Application No.

10/540,934

Applicant(s)

HARMON, JOHN W

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 24 July 2007.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-44 is/are pending in the application.
- 4a) Of the above claim(s) 8-13, 16 and 25-40 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-7, 14, 15, 17-24 and 41-44 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                                | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This Office action is in response to the communication filed 7-24-07.

Claims 1-44 are pending in the instant application.

Claims 8-13, 16 and 25-40 have been withdrawn previously from consideration, claims 1-7, 14, 15, 17-24, 41-44 have been examined on their merits as set forth below.

#### ***Continued Examination Under 37 CFR 1.114***

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 7-24-07 has been entered.

#### ***Response to Arguments and Amendments***

Applicant's arguments and declaration (evidence) filed 7-24-07 with respect to claims 1-7, 14, 15, 17-24, 41-44 have been considered but are moot in view of the new ground(s) of rejection set forth below.

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

New Rejections

**Claim Rejections - 35 USC § 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-7, 14, 15, 17-24 and 41-44 are rejected under 35 U.S.C. 103(a) as being unpatentable over the combination of Zhang et al (USPN 6,972,013), Glasspool-Malone et al (Mol. Therapy, Vol. 2, pages 140-146 (2000)) and Bureau et al (USPN 6,528,315), the combination in view of Ruben et al (US 2003/0186904), the combination further in view of Arbeit (USPN 6,838,430), Blott et al (US 2007/0141128) and Miller (USPN 4,846,181).

The claims are drawn to a method to promote wound healing in a patient comprising administering a plasmid nucleic acid encoding a growth factor operably

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linked to a promoter, which growth factor is optionally HIF-1 $\alpha$ , to a cutaneous wound site, and applying an electric field intradermally to the wounded tissue, which electric field comprises 6-18 square wave pulses, at 400-1800 V/cm, from 100 microseconds to 20 milliseconds in duration, wherein the wound eschar is removed surgically prior to administering the nucleic acid, and wherein the wound is a decubitus ulcer or a burn wound, and wherein the patient is a diabetic.

Zhang (USPN 6,972,013) teaches intradermal delivery of plasmid DNA encoding at least one growth factor, operably linked to a promoter, for acceleration of wound healing, followed by electroporation using single square wave pulses between 100-500 V/cm, between 5 microseconds and 99 milliseconds (see esp. col. 3, col. 4, figure 11, col. 7, 8, 11, 12, 15, 21 and 45).

Glasspool-Malone (Mol. Therapy, Vol. 2, pages 140-146 (2000)) teaches improving the intradermal delivery of nucleic acids to cells in a subject using a pin electrode (see pages 140-141).

Bureau (USPN 6,528,315) teaches delivery of at least one transgene encoding a growth factor to cells using electroporation, optionally using an intensity between 200 and 600 V/cm for a total duration greater than 10 milliseconds, with square wave pulses from 1- 1000 pulses (see col. 3-4, 6 and 24).

The primary references of Zhang, Glasspool-Malone and Bureau do not teach the treatment of burns or decubitus ulcers in diabetics, nor do they teach the administration of HIF-1 $\alpha$  for wound healing, nor the removal of eschar prior to administration of the nucleic acid.

Ruben (US 2003/0186904) teaches the use of electroporation for recombinant gene delivery to target cells, and teaches the use of growth factors for treating wounds, burns and other skin disorders in diabetics, including the administration of the growth factor, KGF-2, in combination with one or more additional nucleic acids encoding therapeutic agents that promote wound healing (see pages 1, 64-69, 88-89 and 134).

Arbeit (USPN 6,838,430) teaches the administration of a nucleic acid encoding HIF-1 $\alpha$  to accelerate wound healing in a patient (col. 2-3 and 8).

Blott (US 2007/0141128) teaches the removal of materials deleterious to wound healing from the wound site, including removing and limiting eschar and necrotic cells from the wound bed (see paragraph 0065 on p. 3). Blott also teaches the retention and administration of beneficial materials, including nucleic acids encoding therapeutic molecules, to the wound bed and edges of the wound for promoting efficient healing, especially for diabetic foot ulcers and decubitus ulcers (see pages 1-3, 6, 14, 15, 24, claims 3 and 4).

Miller (USPN 4,846,181) teaches the historical approach of applying pulsed electrical fields intradermally to wounded tissues for promoting wound healing in a subject (see the abstract; col. 4-5, Tables I-XX and col. 25).

The instant invention would have been obvious to one of ordinary skill in the art because the administration and expression of nucleic acids encoding wound healing polypeptides at the site of the wound (and using electroporation for enhancing nucleic acid delivery to cells in the wound area) were well known to accelerate wound healing, as taught previously by many, including Zhang, Reuben, Blott and Arbeit. Furthermore,

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it would have been obvious to enhance nucleic acid delivery to target cells, including to cells and tissues at wound sites, using electocurrent because electroporation of cells in vitro and in vivo was well known in the art for enhancing nucleic acid delivery as taught previously by Zhang, Glasspool-Malone, Bureau and Ruben. And Miller taught the use of applying electric current to wounds to stimulate wound healing more than twelve years before the filing of the instant application.

One of ordinary skill in the art would have expected that the application of electric current under the well known and previously described conditions set forth by Zhang, Glasspool-Malone, Bureau, Ruben and Miller would have enhanced delivery of wound healing therapeutics to the wound site and enhance the healing process. One of ordinary skill in the art would have expected that the delivery of nucleic acids encoding growth factors including HIF-1 $\alpha$  and KGF to the site of the wound, including to the peripheral wound tissues and intradermally, would enhance the healing process because the use of these growth factors in wound healing had been taught previously by Zhang, Ruben and Arbeit. What's more, Blott and Miller had taught that the allogeneic wound healing factors and polypeptides (present at the sight of the wound) also enhance wound healing, including after application of electric current to the wound area.

One would have been motivated to utilize these wound healing approaches, including application of electric current under the conditions claimed, including the administration of recombinant nucleic acids encoding wound healing factors to the wound area, to wounds in a diabetic and to decubitus ulcers because these wounds are

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slow to heal and enhancing the healing process reduces permanent tissue damage in diabetics. One of ordinary skill in art would have also been motivated to mechanically remove necrotic cells and eschar from the wound area because this was taught previously by Blott to enhance the healing process because necrosis and eschar are known to slow the healing process. One of ordinary skill in the art would also have been motivated to utilize the techniques of the instant invention in treating burn wounds because enhancing wound healing in burn patients enhances their chances of survival, and reduces pain and suffering, especially in instances where regenerative properties are compromised in a patient (e.g. large burn areas, or in diabetics). For these reasons, the instant invention would have been obvious to one of ordinary skill in the art at the time the invention was made.

### ***Conclusion***

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. ' 1.6(d)). The official fax telephone number for the Group is 571-273-8300. NOTE: If Applicant does submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.



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Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jane Zara whose telephone number is (571) 272-0765. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on (571) 272-0763. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

**Jane Zara**  
**9-25-07**

JANE ZARA, PH.D.  
PRIMARY EXAMINER